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PATENT
Docket No. 20784/6

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10/23/02

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Hans-Ulrich Demuth, Torsten Hoffmann, Dagmar Schlenzig and
Ulrich Heiser

Application No.: 10/082,001 Examiner: Unknown

Filed: February 22, 2002 Group: 1646

For: *New Effectors of Dipeptidyl Peptidase IV for Topical Use*

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 on:

By:

Deborah Celeste

Date

May 21, 2002

**TRANSMITTAL OF ENGLISH TRANSLATION OF
INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

Assistant Commissioner for Patents
Washington, D.C. 20231

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Sir:

The above-referenced patent application claims priority, pursuant to 35 U.S.C. §120, from PCT/EP 00/08118, filed on August 20, 2000 which also claims priority pursuant to 35 U.S.C. §119 to DE 199 40 130.6 filed on August 24, 1999. To perfect this claim of priority, Applicant hereby submits a copy of the English Translation of the International Preliminary Examination Report.

Dated:

5/21/02

Respectfully submitted,

By:

Mark A. Hofer

Reg. No. 30,068

Attorney for Applicants

Customer Number: 21710

Brown Rudnick Berlack Israels, LLC

One Financial Center

Boston, MA 02111

Tel: 617-856-8327

Fax: 617-856-8201

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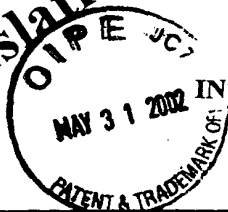
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PATENT COOPERATION TREATY

PCT

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Translation



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

7

Applicant's or agent's file reference ./.	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/08118	International filing date (day/month/year) 20 August 2000 (20.08.00)	Priority date (day/month/year) 24 August 1999 (24.08.99)
International Patent Classification (IPC) or national classification and IPC C07C237/00		
Applicant PROBIODRUG AG		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>1</u> sheets.</p>	
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input checked="" type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input checked="" type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input checked="" type="checkbox"/> Certain documents cited</p> <p>VII <input checked="" type="checkbox"/> Certain defects in the international application</p> <p>VIII <input checked="" type="checkbox"/> Certain observations on the international application</p>	

Date of submission of the demand 12 March 2001 (12.03.01)	Date of completion of this report 16 November 2001 (16.11.2001)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP00/08118

I. Basis of the report

1. This report has been drawn on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

- ☐ the international application as originally filed.
- ☒ the description, pages 1-20, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.
- ☒ the claims, Nos. 1-14, 20-27, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 15-19, filed with the letter of 03 October 2001 (03.10.2001),
Nos. _____, filed with the letter of _____.
- ☒ the drawings, sheets/fig 1/1, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: I

I Amendments (PCT Rule 70)

The applicant has excluded Examples 2 and 3 of document D2 from Claim 15 by means of disclaimers.

These disclaimers are allowed.

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II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
 - ☐ copy of the earlier application whose priority has been claimed.
 - ☐ translation of the earlier application whose priority has been claimed.
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

See annex

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.
PCT/EP 00/08118

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: II

II Priority (PCT Article 8)

The priority claim of the present application is valid,
having regard to the filing date of the German patent
application 19940130.6 (24.08.1999).

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV

IV Unity of invention (PCT Rule 13)

The following groups of claims are identified:

- A) compounds of general formula A(B)-(C), and the use thereof (Claims 1 - 14), and
- B) compositions containing a compound of general formula A(B)-(C) and an adjuvant, and the use thereof (Claims 15 - 27).

These groups are not so linked as to form a single general inventive concept (PCT Rule 13.1) for the following reasons:

Both the above-mentioned groups contain a compound of general formula A(B)-(C). However, the definition of B in Claim 1 is inconsistent with that of Claim 15. The compounds defined in Claim 1 are therefore not identical to those of Claim 15. Consequently, these claims lack unity of invention (PCT Rule 13).

In the following explanations, reference is therefore made to Invention I (claims 1 - 14) and Invention II (Claims 15 - 27).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	Inventions I & II	YES
	Claims		NO
Inventive step (IS)	Claims	Inventions I & II	YES
	Claims		NO
Industrial applicability (IA)	Claims	Inventions I & II	YES
	Claims		NO

2. Citations and explanations

Explanation (PCT Rule 66(2)).Subject matter of the present application.

A compound of general formula A(B)-(C), a composition containing a compound of general formula A(B)-(C), and the use thereof in drugs for the topical treatment of diseases in which the activity of DPP-IV is important.

Citations (PCT Rule 64.1)

D1: WO-A-95/34538.

D2: WO-A-95/15309.

D1 discloses the purification of DPP-IV and inhibitors of DPP-IV. The inhibitors of D1 are C-terminal pyrrolidine-modified amino acids of general formula A-C. The difference between the inhibitors known from D1 and the inhibitors presented in the present application is that the side chain of the amino acid is not modified.

The DPP-IV inhibitors of D2 are of general formula A(B)-(C). The amino acids Glu, Lys and Thr cited in Examples 2 to 4 are modified both on the C terminus with a pyrrolidine group and on the side chain. Furthermore, compounds 55 and 125 disclosed in D2 are glycine-modified

.../...

(Continuation of V.2)

compounds of formula Glu(Gly)-pyrrolidine and Lys(Gly)-pyrrolidine. Example 2 shows a compound which is covered by the definition of the general formula A(B)-(C).

Novelty (PCT Article 33(2)).

Invention I:

The compounds of Invention I are regarded as novel in relation to D1 and D2.

Invention II:

Examples 2 and 3 of D2 are excluded by means of disclaimer from the subject matter of Claim 15. The subject matter of Invention II is therefore regarded as novel.

Inventive step (PCT Article 33(3)).

Inventions I & II:

There are no hints of any kind in D1 and D2 as to how a person skilled in the art should adapt the known compounds in order to improve the activity in drugs which are intended solely for topical applications.

The presence of an inventive step in Inventions I & II is confirmed.

Industrial applicability (PCT Article 33(4)).

The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of the subjects of Claims 11 - 14 and 25 - 27 in their present form.

Patentability may depend on the wording of the claims. The EPO, for example, does not recognize the industrial applicability of claims to the medical use of a compound; it does, however, allow claims to the first medical use of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No.
Patent No.

Publication date
(day/month/year)

Filing date
(day/month/year)

Priority date (valid claim)
(day/month/year)

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)

Date of written disclosure
referring to non-written disclosure
(day/month/year)

See annex

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: VI

VI Cited documents (PCT Rule 64.3).

D3: DE-A-198 26 972 23 December 1999.

D3 discloses DPP-IV inhibitors of formula A(B)-(C) and the use thereof in drugs. Claims 5 - 9 disclose the use of inhibitors which are covered by the description of Claim 15 of the present application (e.g., Nε-4-nitrobenzyloxycarbonyl-L-Lys-thiazolidide).

D3 is therefore prejudicial to novelty for Claims 15 - 27 (Invention II).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

**Observations concerning the description (PCT Article 5,
PCT Rule 9).**

The applicant has forgotten to delete an obviously internal
note from the description ['Should this not be A?']
(page 7, line 6).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 00/08118

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Observations on the claims (PCT Article 6).

Claims 2 - 4, 6 and 20 are not supported by the description.
Only compositions are mentioned on page 5 (lines 10 - 13),
but not compounds A(B)-C according to Claim 1.